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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,661	ZHANG ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,9-13,19-21 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7, 9-13* is/are allowed.

6)☒ Claim(s) *1,3-5,19-21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3-5, 7, 9-13, 19-21 and 26 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claims 1, 3-5 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's amendment of the claims.

Claim Rejections - 35 USC § 112

4. Claims 1, 3-5, 19-21 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 16 February 2006, as applied to claims 1, 3-5, 7, 9-13 and 19-21. Applicant's arguments filed 16 June 2006 have been fully considered but they are not persuasive.

A full review of the specification indicates that nucleic acids encoding bacterial autoinducer inactivation proteins are essential to the operation of the claimed invention. As the protein and its activity are novel, then is no well-developed field of prior art.

The claims are drawn to a genus of bacterial autoinducer inactivation protein-encoding nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2 under hybridization conditions in which only the wash is described; thus, the claim is very broad.

The specification does not describe any structural characteristics of the claimed nucleic acids. The structural features that distinguish bacterial autoinducer inactivation protein-encoding nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2 from other nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2 are not described in the specification. The specification provides no description of how the structure of SEQ ID NO:2 relates to the structure of other bacterial autoinducer inactivation proteins. The specification describes no structure required for the recited function, and the necessary and sufficient structural elements of a protein with bacterial autoinducer inactivation proteins are not described.

The only species described in the specification is SEQ ID NO:1, which encodes SEQ ID NO:2. One of skill in the art would not recognize that Applicant was in possession of the necessary common attributes or features of the genus in view of the disclosed species. Thus, since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 alone is insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described nucleic acids that encode a bacterial autoinducer inactivation protein within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that they have satisfied this requirement because the have shown using Southern analysis that the claimed nucleic acid is conserved in many Bacillus strains (response pg 5).

This is not found persuasive because the specification does not descrinbe the structural features of these nucleic acid, and none were cloned at the time of filing.

Applicant urges that Dong et al (2002) shows that clones have 90-94% similarity (response pg 5).

This is not found persuasive because the necessary and sufficient structural features of nucleic acids that encode AiiA proteins are not described in the specification within the full scope of the claims. Dong et al is a post-filing reference, and thus, cannot be relied upon to describe the claimed nucleic acids.

5. Claims 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is directed to a specific Bacillus strain, 240BJ. Since 240BJ is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the strain is not so obtainable or available, a deposit of it may satisfy the requirements of 35 USC 112. The specification does not disclose a

repeatable process to obtain the strain and it is not apparent if the strain is readily available to the public. Thus, a deposit is required for enablement purposes.

If a deposit is made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make the same, or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.801 - 1.809 [MPEP 2401-2411.05] for additional explanation of these requirements.

6. Claims 1, 3-5, 19-21 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:2, vectors comprising them, cells transformed with the vector and a method of using the nucleic acids to increase disease resistance in a plant, does not reasonably provide enablement for bacterial autoinducer inactivation protein-encoding nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2, vectors comprising them, cells transformed with the vector and a method

of using the nucleic acids to increase disease resistance in a plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 16 February 2006, as applied to claims 1, 3-5, 7, 9-13, and 19-21. Applicant's arguments filed 16 June 2006 have been fully considered but they are not persuasive.

The claims are broadly drawn to bacterial autoinducer inactivation protein-encoding nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2, vectors comprising them, cells transformed with the vector and a method of using the nucleic acids to increase disease resistance in a plant.

The instant specification, however, only provides guidance for isolation of SEQ ID NO:1, which encodes SEQ ID NO:2, from bacterial isolate nonpublically available 240B1 (pg 12-17); and expression in *Erwinia carotovora* to produce a strain with decreased virulence on plants (pg 17-18).

The instant specification fails to provide guidance for bacterial autoinducer inactivation protein-encoding nucleic acids that hybridize to any nucleic acid that encodes SEQ ID NO:2, vectors comprising them, cells transformed with the vector and a method of using the nucleic acids to increase disease resistance in a plant.

The instant specification fails to provide guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain lactonase activity of the encoded protein. The specification also fails to

provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids that hybridize to SEQ ID NO:1 or that hybridize to any nucleic acid that encodes SEQ ID NO:2. Making all possible single amino acid substitutions in an 250 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{250} nucleic acids. Because nucleic acids that hybridize to SEQ ID NO:1 or that hybridize to any nucleic acid that encodes SEQ ID NO:2 would encode proteins with many amino acid substitutions, many more than 19^{250} nucleic acids would need to be made and analyzed.

Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with many amino acid substitutions that also have bacterial autoinducer inactivation activity would require undue experimentation.

As the specification does not describe the transformation of any plant with a nucleic acid that hybridizes to any nucleic acid that encodes SEQ ID NO:2, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with increased disease resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that Molina teaches the results of two bacterial autoinducer enzymes, not autoinducer inactivation enzymes (response pg 6).

This portion of the rejection is withdrawn.

Applicant urges that Dong et al (2001) teaches that the nucleic acid confers strong disease resistance in transgenic plants (response pg 6).

This portion of the rejection is withdrawn.

7. Claims 7 and 9-13 are allowed.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
August 18, 2006